Translation

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY
(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference ONF-4826PCT	**FOR FURTHER ACTION**	See Form PCT/IPEA/416
International application No. PCT/JP2003/015718	International filing date (*day/month/year*) 09 December 2003 (09.12.2003)	Priority date (*day/month/year*) 10 December 2002 (10.12.2002)
International Patent Classification (IPC) or national classification and IPC C07D213/74, 401/14, 403/04, 403/14, 471/04, 401/12, 401/04, 403/12, 405/14, 409/14, 417/14, 405/14, 409/14, 417/14, 405/12, 413/04, 413/12, 215/42, 493/04, 493/10		
Applicant ONO PHARMACEUTICAL CO., LTD.		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 9 sheets, including this cover sheet.

3. This report is also accompanied by ANNEXES, comprising:

   a. ☐ *(sent to the applicant and to the International Bureau)* a total of _____ sheets, as follows:

      ☐ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).

      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.

   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s)) _____, containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:

   ☒ Box No. I Basis of the report
   ☐ Box No. II Priority
   ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   ☒ Box No. IV Lack of unity of invention
   ☒ Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   ☒ Box No. VI Certain documents cited
   ☐ Box No. VII Certain defects in the international application
   ☒ Box No. VIII Certain observations on the international application

Date of submission of the demand 11 June 2004 (11.06.2004)	Date of completion of this report 04 November 2004 (04.11.2004)
Name and mailing address of the IPEA/JP Facsimile No.	Authorized officer Telephone No.

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
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Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ This report is based on translations from the original language into the following language _____, which is language of a translation furnished for the purpose of:

☐ international search (under Rules 12.3 and 23.1(b))

☐ publication of the international application (under Rule 12.4)

☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the **elements** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

☒ The international application as originally filed/furnished

☐ the description:

pages _____, as originally filed/furnished

pages* _____ received by this Authority on _____

pages* _____ received by this Authority on _____

☐ the claims:

pages _____, as originally filed/furnished

pages* _____, as amended (together with any statement) under Article 19

pages* _____ received by this Authority on _____

pages* _____ received by this Authority on _____

☐ the drawings:

pages _____, as originally filed/furnished

pages* _____ received by this Authority on _____

pages* _____ received by this Authority on _____

☐ a sequence listing and/or any related table(s) – see Supplemental Box Relating to Sequence Listing.

3. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages _____

☐ the claims, Nos. _____

☐ the drawings, sheets/figs _____

☐ the sequence listing *(specify)*: _____

☐ any table(s) related to sequence listing *(specify)*: _____

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

☐ the description, pages _____

☐ the claims, Nos. _____

☐ the drawings, sheets/figs _____

☐ the sequence listing *(specify)*: _____

☐ any table(s) related to sequence listing *(specify)*: _____

* *If item 4 applies, some or all of those sheets may be marked "superseded."*

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Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application.

☒ claim No. 31

because:

☒ the said international application, or the said claim No. 31 relates to the following subject matter which does not require an international preliminary examination *(specify)*:

The invention of claim 31 includes treatment of the human body by therapy.

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. _____ are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. _____ are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for said claim No. 31.

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form
- ☐ has not been furnished
- ☐ does not comply with the standard

the computer readable form
- ☐ has not been furnished
- ☐ does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ see Supplemental Box for further details.

Box No. IV Lack of unity of invention

1. ☐ In response to the invitation to restrict or pay additional fees the applicant has:

   ☐ restricted the claims.

   ☐ paid additional fees.

   ☐ paid additional fees under protest.

   ☐ neither restricted nor paid additional fees.

2. ☒ This Authority found that the requirement of unity of invention is not complied with and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is

   ☐ complied with.

   ☒ not complied with for the following reasons:

The general formula of the compounds of claim 1 does not have a consistent basic scaffold and in its entirety is represented by variable groups that contain a plurality of selection branches. The only structural special feature held in common by the compounds represented in this general formula is that they have a cyclic structure that is directly linked to the nitrogen atom of a nitrogen-containing heterocyclic ring. However, as described in WO 01/040227, compounds having a cyclic structure that is directly linked to the nitrogen atom of a nitrogen-containing heterocyclic ring are publicly known, and it is widely known that such compounds have an antagonistic effect on chemokine receptors. Thus, after consideration of the contribution to prior art, this examination finds that the aforementioned structural special feature does not constitute a special technical feature, and the compounds of claim 1 do not have a common special technical feature.

Therefore, the invention of claim 1 is not so linked as to form a single general inventive concept.

This examination also finds that the inventions of claims 2-30 and 32 as well do not share a special technical feature and do not constitute a group of inventions so linked as to form a single general inventive concept.

4. Consequently, this report has been established in respect of the following parts of the international application:

   ☐ all parts.

   ☒ the parts relating to claims Nos. 1-30, 32 .

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Box No. V **Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

Novelty (N)	Claims	9, 19-24, 26, 28-30	YES
	Claims	1-8, 10-18, 25, 27, 32	NO
Inventive step (IS)	Claim	9	YES
	Claims	1-8, 10-30, 32	NO
Industrial applicability (IA)	Claims	1-30, 32	YES
	Claims		NO

2. Citations and explanations (Rule 70.7)

Documents
1. WO 00/56729 A1 (ANORMED INC.) September 28, 2000 & EP 1163238 A1
2. WO 02/22599 A2 (ANORMED INC.) March 21, 2002 & EP 131451 A1
3. WO 01/40227 A1 (Ono Pharmaceutical Co., Ltd.) June 7, 2001 & EP 1236726 A1
4. JP 2002-348288 A (Ono Pharmaceutical Co., Ltd.) December 4, 2002 (Family: none)
5. WO 02/45652 A2 (MERCK & CO.) June 13, 2002 & US 2002/137755 A1 & EP 1341540 A2
6. Journal of Medicinal Chemistry, March 1968, Vol. 11, No. 2, p. 392-395
7. GB 1113918 A (FARBENFABRIKEN BAYER AKTIENGESELLSCHAFT) May 15, 1968 (Family: none)

<Documents 1 and 2>
Claims 1-8, 10-30, and 32

Although the inventions of claims 1-8, 10-30 and 32 are novel with respect to documents 1 and 2 cited in the international search report, they lack an inventive step.

Documents 1 and 2 describe compounds having a CXCR4 receptor inhibiting effect and medications having the same as an active ingredient that are effective in the treatment of HIV infections, immune diseases, and inflammation, etc. (especially, see document 1 pages 4 to 5 pages 7 to 9, and pages 17 to 18; and document 2, pages 6 to 9). In addition, document 1 states that a heterocyclic ring or an amino group can be selected as a substituent of ring A or ring B represented by group X of General Formula (I) of claim 1 (for example, see page 12, lines 18 to 23; page 15, lines 4 to 7, etc.), and document 2 states that a heterocyclic group or an amino group can be selected as a substituent of groups X and Z of General Formula (I) of claim 1 (for example, see page 13a, lines 5 to 9; page 16, lines 8 to 10, etc.) Therefore, the compounds of claims 1-8, the medicine of claims 10-27, and the use for the production of compounds of claim 32 are obvious to persons skilled in the art from the descriptions in documents 1 and 2.

In addition, documents 1 and 2 describe the combined use of a chemokine receptor inhibitor and another ingredient for the treatment of HIV such as a reverse transcriptase inhibitor or protease inhibitor, etc. Therefore, the medicine of claims 28-30 is obvious to persons skilled in the art.

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Box No. VI Certain documents cited

1. Certain published documents (Rule 70.10)

Application No. Patent No.	Publication date *(day/month/year)*	Filing date *(day/month/year)*	Priority date (valid claim) *(day/month/year)*
WO 03/062236 A1	31.07.2003	10.01.2003	22.01.2002
EX			

2. Non-written disclosures (Rule 70.9)

Kind of non-written disclosure	Date of non-written disclosure *(day/month/year)*	Date of written disclosure referring to non-written disclosure *(day/month/year)*

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

The general formula of the compound of claim 1 does not have a consistent basic scaffold, and in its entirety is represented by variable groups containing a plurality of selection branches, thereby encompassing an extremely large number of compounds. On the other hand when we compare this with the disclosure in the Specification, we find that the invention described in the claim does not satisfy the requirements of PCT Article 5 and PCT Article 6 to the extent that a meaningful prior art search can be performed for the entirety of the claim.

As a result, after consideration of the description in the Specification, this report was prepared restricted to the compound represented by the general formula of claim 6, the compounds of claim 9 and nitrogen-containing heterocyclic ring compounds having a chemokine receptor inhibiting effect.

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.
Continuation of Box :

(Supplemental Box 1)

(Continuation of IPC)
C07D495/04, 473/16, 251/50, 239/42, A61K31/55, 31/506, 31/551, 31/4725, 31/517, 31/553, 31/4709, 31/444, 31/519, 31/506, A61P3/00, 9/00, 25/00, 29/00, 31/00, 31/18, 35/00, 37/00, 37/08, 43/00

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.
Continuation of Box V:
(Supplemental Box 2)

<Documents 3 and 4>
Claims 1-3, 10-18, 27 and 32

Based on the descriptions in documents 3 and 4 cited in the international search report, the inventions of claims 1-3, 10-18, 27 and 32 lack novelty and an inventive step.

Documents 3 and 4 describe compounds included in the general formulas of the compounds of claims 1 -3 that have a chemokine inhibitory action and the use of said compounds as the active ingredient of a medicine that is useful for the treatment of HIV infections and the treatment of immune diseases, etc. [especially, see document 3, pages 184 to 185, page 304, pages 311 to 312, page 320, page 328, page 336, page 343, pages 344 to 345, pages 351 to 352, pages 359 to 362, and page 378; as well as document 4, page 33, Compound 2(33), page 32, Compound 2(54), and page 36, Compound 2(62)].

Therefore, the compounds of claims 1-3, the medicine of claims 10-18, and 27, and the use for the production of compounds of claim 32 are identical to the inventions described in documents 3 and 4.

<Documents 5-7>
Claims 1-8, 10-18, 25, 27, and 32

Based on the descriptions in documents 5-7 cited in the international search report, the inventions of claims 1-8, 10-18, 25, 27 and 32 lack novelty and an inventive step.

Documents 5-7 describe a nitrogen-containing heterocyclic ring having a substituted amino group and an azepin-1-yl group (especially, see document 5, page 105, Compound 25-4; document 6, page 393, Compound 23; and document 7, page 5, compound k). Therefore, the novelty and inventive step of the compounds of claims 1-8 are refuted by the descriptions in documents 5-7.

In addition, document 5 states that the above compound is useful in the in treatment of inflammatory diseases, and therefore the medicine of claims 10-18 and 27 and the use for the production of compounds of claim 32 are identical to the inventions described in document 5.

Document 6 states that the above compound is a substance that affects the nerves. Therefore, the medicine of claims 10-18, 25, and 27, and the use for the production of compounds of claim 32 are identical to the inventions described in document 6.

<Documents 1-7>
Claim 9

The invention of claim 9 has novelty and involves an inventive step with respect to documents 1-7.

The compound of claim 9 is not obvious to persons skilled in the art from the descriptions in documents 1-7.